



National  
Multiple Sclerosis  
Society

**MS Learn Online  
Feature Presentation  
Disease Modifying Therapies – Part Two  
Fred Lublin, MD**

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**Tom>>** Welcome to MS Learn Online, I'm Tom Kimball.

**Tracey>>** And I'm Tracey Kimball. We're back with Dr. Fred Lublin who will continue his conversation on disease modifying therapies.

**Tom>>** That's right. In this program he'll discuss Novantrone and Tysabri but first he'll answer a commonly asked question.

**>>Rick Sommers:** Doctor, once one of your patients starts on therapy, how long are they on it?

**>>Dr. Lublin:** They're on it until something better comes along. Somebody asks the question all the time, how long am I going to be on this or that? And it's either until something better comes along, which we're hopeful for, or we determine that we don't think it's working for them, or they don't tolerate it, in which case we would have to switch.

**>> Rick Sommers:** There are simple measures that a person can take to alleviate some of the side effects and discomforts in the therapies they use. What are some of them?

>>**Dr. Lublin:** Well, one is proper injection technique training, and that helps a great deal. The other is trying to alleviate some of the symptoms, such as the flu-like symptoms which could be mitigated with things like ibuprofen and acetaminophen. You know, Tylenol and Motrin, and things of that sort. And timing of the injections also can make a difference. For example, taking them before bedtime so you can sleep through some of the side effects.

>> **Rick Sommers:** From your patients and your experience, any difference between some of the patients who use an auto-inject, which is available for some of the therapies, as opposed to doing an injection themselves?

>>**Dr. Lublin:** By and large, our group likes the auto-injectors but there are still some people who say, no, I don't like it at all, I'd rather give myself the injection. So, it's an individual and personal thing.

>> **Rick Sommers:** I want to talk to you about Novantrone and Tysabri, which are different therapies, and let's start first with Novantrone.

>>**Dr. Lublin:** So, Novantrone is indicated for worsening forms of MS. So, that means bad relapsing-remitting MS and secondary-progressive MS, and an unusual form called progressive-relapsing MS. It's a chemotherapeutic agent. It's given as an intravenous infusion every three months, and it has reasonably good clinical trial data, suggested it works in this particular group of patients. That's how it got approved. And so it's been used. We've been using it.

There are some more serious side effects with Novantrone. One is you only can take it for 33 months. That's the full course. Because after that there is a cumulative risk of damage to the heart muscle.

>> **Rick Sommers:** Okay.

>>**Dr. Lublin:** And so that's as much as we'll give. And, in fact, while you're taking it you have to be monitored before each injection -- infusion, rather -- to make sure that the heart muscle is pumping optimally. And then after you stop it you still have to be monitored for what's called cardiac output, pretty much for the rest of your life.

The other small risk with Novantrone is of what's called secondary leukemia, that is, leukemia that results from a chemotherapeutic agent. It's a well-known phenomenon. The risk is low, 1% to 2% as we're seeing it now, although people are starting to report more of it than we originally thought. But it's a serious disease when you get it. So, that's a worry.

Any chemotherapeutic agent, you also worry about infections because it lowers your white blood cell count, lowers your resistance as such. But it is the only approved agent in that class of disease.

>> **Rick Sommers:** Okay. And Tysabri?

>>**Dr. Lublin:** So, Tysabri is also given as an infusion. It's what is called a monoclonal antibody. It's approved for relapsing forms of MS. It's given every four weeks as an infusion. Has very good clinical trial data, which led to its approval, and its major side effects are (a) infusion reactions and (b) infections, funny infections, the most notable of which is something called progressive multifocal leukoencephalopathy, which is a mouthful, or PML. PML is a serious infection of the brain that was reported late in the developmental phase of Tysabri and now is being followed very carefully, because the use of Tysabri in the United States is under a controlled program where everyone has to register and be kept track of.

The figure for the incidents of PML is somewhere between 1 in 1,000 and 1 in 10,000, and it's still popping up about that range. But the drug is otherwise doing very well. Effective, very effective. Many of us use it,

most of us use it in individuals who haven't tolerated or haven't responded to either Interferon or Copaxone.

>>**Rick Sommers:** Those therapies are designed for relapsing-remitting candidates. What do you say to somebody who comes in and who is a primary-progressive patient?

>>**Dr. Lublin:** We have no approved therapies for primary-progressive MS, and what we have is not very good for any form of progressive MS. And so it's our biggest unmet therapeutic need is to try and develop something for primary-progressive MS. It's more difficult to treat and it's more difficult to study. So, we've had a couple of very well designed trials that failed to show an effect of their agents. There is at least one study underway now for primary-progressive MS, and at least one for secondary - progressive MS. So, we're hopeful of finding something for progressive disease, but right now we don't have anything that's available. So, people try a whole host of things, but nothing that's approved.

>> **Rick Sommers:** What else besides disease-modifying therapies can you offer?

>>**Dr. Lublin:** So, we're in the happy position of being able to be truly holistic for patients with MS in that we have at our care centers the ability to look at all aspects of the disease. So, we've talked a lot about disease-modifying therapies, which are at the forefront of our thinking, but in addition to that we treat the exacerbations when they come up usually with high-dose steroids. We have techniques to enhance recovery beyond steroids. Things like plasmapheresis, which given right after an attack can enhance recovery. We have molecules in the pipeline and one now in the hands of the FDA, that enhance function, that is, improve conduction through partially demyelinated or damaged nerves.

And then we have symptom management. And symptom management is extremely important, because no matter where someone is in the spectrum

of the disease, from very, very mild to very, very disabled, there's a whole host of additional things in addition to just the MS itself that we treat things like bladder dysfunction and bowel difficulties and sexual dysfunction, psychological issues and psychiatric, like depression; skin issues, swallow and speech difficulties, fatigue, tremors. I mean, it's a very, very long list, and the complications of our therapy.

And so all of those have to be dealt with as part of the team, and some of them we deal with ourselves, some of them involve our colleagues in urology, some our colleagues in physical medicine and rehabilitation, and many others. And so the opportunity of taking care of the whole individual is there and is very important for us to do.

>> **Rick Sommers:** The one thing that I really glean from this is it's a real team effort. It really -- we're relying not on one person, not solely on your shoulders, but on a team. As you mentioned, social workers and other kinds of therapists.

>>**Dr. Lublin:** Optimal MS care is very much a team. There are many people involved, so there is the neurologist and the physiatrist and the psychiatrist, internist, nurses and nurse practitioners, social workers, psychologists, I mean, psychiatrists. There are many and it's a disease that affects all of the nervous system, so it affects everything that could be done with the body and involves many people.

>> **Rick Sommers:** You're pretty upbeat, though.

>>**Dr. Lublin:** I am. We've seen enormous changes over the time when we had no therapies or just treating exacerbations. Now we can treat all the things that I just mentioned, plus we have a pipeline full of really interesting and promising molecules to take us into the next generation.

And then we have a couple of near and far horizons. We have the near horizon of looking to see if we can employ neuroprotective strategies,

strategies and molecules. So, we hope it would salvage and save neurons, nerve cells and axons from damage.

And then a little farther into the future repair of the damaged nervous system, whether it be stem cells or some other cell that's going to be involved in repair. But these are all moving along the developmental pathways.

**Tom>>** Thank you Dr. Lublin for helping us to better understand what disease modifying therapies are available for many people with MS.

**Tracey>>** If you're interested in learning more, you can find additional information on any of the therapies on the National MS Society website.

**Tom>>** Thanks for joining us.